Advances in the structure of bacterial chemotaxis signaling

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A vital function of bacterial chemosensory arrays is the transmembrane signal transduction of methyl-accepting chemotaxis proteins (MCPs). By biasing their migration in the direction of favorable conditions, the chemosensory arrays enable bacteria to react to changes in their surroundings. MCPs, CheA, and CheW proteins make up the chemosensory array's core signaling unit (CSU). Changes in bacterial motility result from attractant molecules binding to the cytosolic kinase CheA, which is transduced via the MCPs that bridge the inner membrane of the bacteria. However, it has been difficult to evaluate several proposed models for MCP activity due to a lack of structural evidence (Riechmann & Zhang, 2023).

Advancements in Understanding Array Structure with CryoET

The structure and functionality of bacterial chemosensory arrays have been better understood thanks to studies employing cryo-electron tomography (cryoET). Chemosensory arrays can be studied in their natural habitat with cryoEMT, yielding insightful results. X-ray crystallography has been used in earlier research to examine discrete MCP domains; nonetheless, the entire MCP structure remains unsolved. For structural research, MCPs' hydrophobic transmembrane domain and flexible sections have presented difficulties (Riechmann & Zhang, 2023).

To overcome these challenges, cryoET has emerged as the primary method for studying MCPs. By imaging bacterial cells, the characteristic array structure can be easily identified and studied in situ. Preparative techniques such as partial lysis of bacterial cells or the use of mutated Min systems can produce thin specimens for cryoET. Recent developments in data acquisition and image processing have significantly improved the resolution of cryoET maps of chemosensory arrays, allowing for the identification of protein secondary structure elements (Riechmann & Zhang, 2023).

Insights into MCP Arrangement and Function from High-Resolution CryoET Maps

These cryoET maps with high resolution have provided fresh perspectives on the layout and operation of MCPs. The distances between MCPs' periplasmic domains indicate contacts between adjacent chemosensory signaling units substrate binding modules, which support cooperativity in signaling. The cytosolic MCP density takes on a straight conformation, defying earlier research that suggested bends at the glycine hinge and HAMP domain (hydrophobic transmembrane domain and two highly flexible regions). The updated maps have also revealed important interactions at the MCP tips and provide light on the location of CheA domains (Riechmann & Zhang, 2023).

Despite these developments, it is still unclear how exactly MCPs transduce signals and what causes the high levels of cooperation among signaling units. High-resolution research is hampered by the pliability of the baseplate's dynamic kinase domains and MCP hinge regions. Time-resolved cryoEM methods and machine learning algorithms could further advance our comprehension of chemosensory arrays. Furthermore, investigating chemosensory systems other than *Escherichia coli* and examining their distinct structural features can yield important information on the function of unknown proteins in more intricate arrays. (Riechmann & Zhang, 2023).

Bacterial chemotaxis coupling protein: composition, roles, and variations

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Coupling proteins create the links between receptors and histidine kinases in most signal transduction systems, which are essential for signal transmission. CheW or CheV are the coupling proteins that are essential to the bacterial chemotaxis mechanism. To establish a core signaling complex, CheW bridges the histidine kinase CheA and the chemoreceptor trimers, among other roles in chemotaxis. In order to create extensive chemosensory arrays that are in charge of gathering and enhancing signals, CheW links CheA activity to chemoreceptor regulation and aids in the formation of linkages between core signaling complexes. CheV works differently in chemotaxis but shares redundant abilities with CheW. Multiple coupling proteins have been identified in various bacteria, such as *E. coli*, *Bacillus subtilis*, *Rhodobacter sphaeroides*, and *Agrobacterium tumefaciens*. The study of chemotaxis in *E. coli* has made it a model organism for understanding chemotaxis systems, and the core signaling complex is conserved among different bacteria (Huang et al., 2019).

The best-studied chemotaxis system is found in *E. coli*, which has six essential components and five transmembrane chemoreceptors. Chemoreceptors sense chemoeffectors, send signals to the histidine kinase CheA, and use the coupling protein CheW to modulate the activity of CheA. Two response regulator proteins, CheY or CheB, receive phosphoryl groups from phosphorylated CheA. These proteins then engage with flagellar motors to rotate the flagella in a clockwise (CW) direction as opposed to a counterclockwise (CCW) manner. To stop the signal, CheZ speeds up phosphorylated CheY's spontaneous dephosphorylation. The methylesterase function of phosphorylated CheB removes methyl groups from some methylable chemoreceptors, reducing MCPs' capacity to activate CheA. By adjusting the methylation status of MCPs, constitutively expressed methyltransferase CheR combines with phosphorylated CheB to reset the activity of CheA and the sensitivity of MCPs to a wide range of environmental stimulus strengths. The structure of MCPs changes in response to an increase in attractant or repellent concentration, which inhibits the autophosphorylation of CheA. Additionally, the amount of phosphorylated CheB in the cell is reduced, which lessens MCP demethylation. CheR continues to methylate MCPs, enhancing MCPs' capacity to stimulate CheA activity, which raises CheY and CheB phosphorylation. Adaptation occurs when the chemotaxis system goes back to its pre-stimulus state (Huang et al., 2019).

As we mentioned early, bacterial chemotaxis systems have two basic architectures: CheW and CheV. CheW is a canonical chemotaxis coupling protein with two subdomains, while CheV is a hybrid protein with an N-terminal CheW-like domain fused to a C-terminal receiver domain that can be phosphorylated. CheW is found in the genomes of completely sequenced bacteria and archaea, while CheV is found in fewer species. Experimental evidence from *Listeria monocytogenes* suggests that CheV can completely substitute for CheW in this bacterium. CheW is present in 95% of genomes with at least one chemotaxis gene, while CheV is found in < 40%. CheW and CheV's genomic locations differ, with one gene usually located near a chemotaxis gene cluster with a cheA gene, and only one cheV in ε- proteobacteria (Huang et al., 2019).

Coupling proteins play a crucial role in bacterial chemotaxis by facilitating the assembly of signaling complexes and chemosensory arrays, allowing bacteria to track spatial gradients of chemoeffectors and move towards optimal environments. The coexistence of multiple coupling proteins in one organism provides flexibility and enhances the organism's ability to adapt to different environmental stimuli. Different coupling proteins may have different roles in chemotaxis; some may behave redundantly, while others may play special, irreplaceable roles. More research is necessary to properly understand the precise regulation and cooperation of numerous coupling proteins in chemotaxis pathways. The various coupling proteins' affinities and expression levels with CheA and chemoreceptors, as well as their unique functions in chemotaxis, require greater investigation (Huang et al., 2019).

References

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